

## LISTING OF CLAIMS

### **Cancel claims 1-28.**

29. (new): A method for detecting a mutation and/or a SNP in a double-stranded test DNA molecule, comprising:

- (a) providing a probe which is a single stranded or double stranded DNA molecule, which probe is optionally detectably labeled, and which probe has (i) a known nucleotide sequence or (ii) a sequence complementary to the sequence of at least a part of the test DNA;
- (b) contacting the probe, after denaturation in the case of a double stranded probe, with a RecA protein which is optionally detectably labeled, to form a RecA filament or filaments;
- (c) contacting the RecA filaments with the test DNA, thereby forming
  - (i) a three stranded DNA D-loop structure, in the case of the single stranded probe or (ii) a four stranded DNA structure in the case of the double stranded probe,
 in the test DNA, which structure comprises the probe strand or strands annealed with the test DNA strands;
- (d) contacting the DNA structure with a MutS protein which is optionally detectably labeled and optionally immobilized, wherein the MutS binds to one or more base pair mismatches or unpaired bases present in the duplex portion of D-loop structure or in the four stranded DNA structure;
- (e) detecting the presence of MutS bound to the DNA structure, or the probe DNA or RecA bound to immobilized MutS,

wherein the presence of the probe DNA or RecA bound to the MutS is indicative of the presence of the mutation or the SNP in the test DNA.

30. (new): The method of claim 29, wherein the mutation being detected is a single nucleotide substitution or the addition or deletion of 1-4 nucleotides.

31. (new): The method of claim 29, wherein the test DNA molecule is selected from the group consisting of prokaryotic genomic DNA, eukaryotic genomic DNA, cDNA, viral DNA, plasmid DNA, and an amplified DNA fragment amplified by PCR or by another amplification method.

32. (new): The method of claim 29, wherein the probe is selected from the group consisting of:
- (a) a synthetic oligonucleotide;
  - (b) a recombinant oligonucleotide;
  - (c) an oligonucleotide obtained by denaturing, and, optionally cleaving, a double stranded DNA molecule.
33. (new): The method of claim 32, wherein the oligonucleotide has a length of about 20 to about 60 nucleotides.
34. (new): The method of claim 29, wherein:
- (i) the probe and the MutS are labeled;
  - (ii) the label is a fluorophore, a chromophore, a radionuclide, biotin or digoxigenin; and
  - (iii) association of the probe label with the MutS label is indicative of the presence of the mutation or the SNP in the test DNA.
35. (new): The method of claim 29, wherein the RecA protein is from *E. coli*.
36. (new): The method of claim 29, wherein
- (i) the RecA and MutS are labeled;
  - (ii) the label is a fluorophore, a chromophore, a radionuclide, biotin or digoxigenin; and
  - (iii) association of the RecA label with the MutS label is indicative of the presence of the mutation or the SNP in the test DNA.
37. (new): The method of claim 29 wherein the MutS is immobilized to a solid support.
38. (new): The method of claim 29 wherein the MutS is detectably labeled, and the detectable MutS label is a fluorophore, a chromophore, a radionuclide, biotin, digoxigenin, a detectably labeled bead, a detectably labeled anti-MutS antibody, or a combination of an unlabeled anti-MutS antibody and a detectably labeled secondary antibody specific for the anti-MutS antibody.
39. (new): The method of claim 29 wherein the RecA protein is labeled and the detection is of the MutS label associated with the RecA label present in the DNA structures.

40. (new): The method of claim 29, wherein the RecA protein is labeled and the detectable RecA label is in the form of a detectably labeled primary anti-RecA antibody, or a combination of an unlabeled anti-RecA antibody and a detectably labeled antibody specific for the anti-RecA antibody.
41. (new): The method of claim 29, wherein one or more of the detectably labeled probe, the detectably labeled RecA and the detectably labeled MutS is labeled with a fluorophore.
42. (new): The method of claim 29, wherein the detecting is by flow cytometry.
43. (new): The method of claim 41 wherein the detecting is by flow cytometry.
44. (new): The method of claim 29 wherein the DNA D loop structure is stabilized by the addition, before step (d), of SSB protein which is optionally detectably labeled.
45. (new): The method of claim 44, wherein,
- (i) the SSB protein is labeled with a detectable label;
  - (ii) the SSB label is a fluorophore, a chromophore, a radionuclide, biotin, digoxigenin, a labeled anti-SSB antibody, or a combination of an unlabeled anti-SSB antibody and a labeled secondary antibody specific for the anti-SSB antibody; and
  - (iii) association of the SSB label with the MutS label is indicative of the presence of the mutation or the SNP in the test DNA.
46. (new): The method of claim 29 or 45 wherein the detecting is by flow cytometry which detects the coincidence of two, three or four labels which are bound to:
- (a) MutS and the probe;
  - (b) MutS and RecA;
  - (c) MutS, RecA and the probe;
  - (d) MutS and SSB;
  - (e) MutS, SSB and the probe; or
  - (f) MutS, SSB, the probe and RecA.
47. (new): The method of claim 29 wherein the probe is labeled by polymerase extension using labeled deoxynucleotide triphosphates or nucleotide terminators.
48. (new): The method of claim 29, wherein the test DNA is immobilized to a solid support

49. (new): The method of claim 29, wherein the probe is bonded to an adduct that allows immobilization of the probe following formation of the D-loop structure or the four-stranded DNA structure.
50. (new): The method of claim 49, wherein the adduct is an oligonucleotide.
51. (new): The method of claim 49, wherein the adduct is biotin or digoxigenin.
52. (new): A kit useful for performance of the method of claim 1, adapted to receive therein one or more containers, the kit comprising:
- (a) a first container containing a RecA protein which is optionally detectably labeled;
  - (b) a second container containing MutS protein which is optionally detectably labeled; and
  - (c) optionally, a third container or plurality of containers containing buffers and reagent or reagents capable of detecting bound MutS.
53. (new): The kit of claim 52 further comprising
- (d) a fourth container, or plurality of containers, containing:
    - (i) a specific oligonucleotide probe or probes, which probes are selected to be complementary to specific sequences in specific regions in the DNA of the sample and which form mismatch-containing or unpaired base-containing heteroduplexes with a mutated or polymorphic sequence or sequences in the specific DNA regions, which probe or probes is or are optionally detectably labeled; and
    - (ii) optionally, an SSB protein which is optionally detectably labeled.
54. (new): The kit of claim 52 or 53 wherein at least one of said RecA protein, said MutS protein, said probe or said SSB protein is detectably labeled.
55. (new) The kit of claim 54 comprising said third plurality of containers containing said reagent which reagent is selected from the group consisting of: (1) a labeled anti-MutS antibody, (2) a labeled anti-RecA antibody, (3) a labeled anti-SSB antibody, and (4) a combination of an unlabeled first anti-MutS, anti-RecA or anti-SSB antibody and a detectably labeled secondary antibody specific for the first antibody.

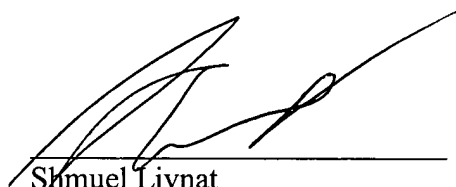
This Preliminary Amendment cancels the original claims (1-28) and replaces them with claims 29-55. This primary purpose of this amendment is to amend the first claim (now claim 29) to include the subject matter of original claims 2-4, to amend most of the remaining multiply dependent claims to depend from claim 29, to amend kit claims 52 and 53 somewhat from their language as original claims 27 and 28, and to add two new dependent kit claims (54 and 55). Several other claims are amended slightly to accord better with the language of new claim 29 and to correct minor spelling or grammatical errors.

As many of the cancelled claims were multiply dependent (typically quadruply-dependent), the total number of claims submitted herewith (30/1 indep.) is significantly lower than the original number of claims (74/6 indep.) paid for. Hence, no additional payment is required.

It is believed that this set of claims, submitted as replacement claims, is more compact, thus making them easier to examine. No new matter is introduced by these amendments. The application is now in condition for examination on the merits.

If any questions remain, the Examiner is encouraged to call the undersigned at (202) 344-8584 to expedite this application.

Respectfully submitted,



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